Treatment Guidelines
from The Medical Letter®

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Drugs for Allergic Disorders

Allergic rhinitis, allergic conjunctivitis, atopic dermatitis, urticaria, anaphylaxis and asthma (not included here; reviewed in *Treatment Guidelines* 2008; 6:83) are prevalent worldwide, especially in industrialized countries. Pharmacologic treatment of these disorders continues to improve in efficacy and safety. In addition to using drugs to prevent and control these allergic diseases, patients should be instructed to avoid, if possible, specific allergens and/or environmental conditions that trigger or worsen their symptoms. Allergen-specific immunotherapy may be useful for treatment of allergic rhinitis and allergic conjunctivitis, and in preventing severe insect venom-triggered reactions.

ALLERGIC RHINITIS

Allergic rhinitis may be seasonal/intermittent or perennial/persistent. H_1-antihistamines, the drugs most commonly used to treat this disorder, are more effective in relieving sneezing, itching and discharge than in relieving nasal congestion.[1]

H_1-Antihistamines – First-generation H_1-antihistamines such as diphenhydramine (*Benadryl*, and others) or chlorpheniramine (*Chlor-Trimeton*, and others) are inexpensive, but even in usual doses they may cause somnolence, interfere with learning and memory, decrease work productivity, impair performance on examinations and other cognitive activities, and increase the risk of on-the-job injuries.[2]

First-generation antihistamines cause CNS adverse effects because they penetrate the blood-brain barrier, bind to H_1-receptors in the brain and interfere with the neurotransmitter effects of histamine. The patient may be unaware of these effects, which can persist in the morning after taking the drug at bedtime and may continue to occur with regular use. First-generation H_1-antihistamines also cause anticholinergic effects such as dry mouth and urinary retention. Administration of the first-generation H_1-antihistamine promethazine (*Phenergan*, and others) to infants and children <2 years old has been associated with respiratory depression and death. Mixtures containing first-generation H_1-antihistamines sold for the relief of cough, colds, allergies and insomnia are no longer approved in the US for children <2 years old or in Canada for children <6 years old. There are also concerns about use of first-generation H_1-antihistamines in the elderly because of their potential for adverse effects and drug-drug interactions.[3]

Second-generation H_1-antihistamines are used as first-line therapy in patients with mild to moderate allergic rhinitis. They penetrate poorly into the brain and are significantly less likely to have CNS adverse effects than first-generation antihistamines. Fexofenadine is free of sedative effects, even in higher-than-recommended doses. Loratadine and desloratadine (an active metabolite of loratadine) are nonsedating in recommended doses; sedation may occur with higher doses. Cetirizine is potentially more sedating than some other second-generation agents. The long-term safety of cetirizine, levocetirizine and loratadine in young children is better established than that of other first- or second-generation antihistamines. It is not clear that levocetirizine offers any advantage over cetirizine.[4,5]

Topical intranasal H_1-antihistamines have a rapid onset of action and are well tolerated. Their clinical efficacy in allergic rhinitis, including some beneficial effects on nasal congestion, appears to be equal or superior to that of oral second-generation H_1-antihistamines.[6,7]

Intranasal Corticosteroids – Topical intranasal corticosteroids are the most effective drugs available for

Table 1. Some Oral Drugs for Allergic Rhinitis

Drug	Formulations	Usual Daily Adult Dosage	Usual Daily Pediatric Dosage
Oral Second-Generation H_1-Antihistamines			
Cetirizine[1] – generic	5, 10 mg chew tabs; 10 mg tabs; 1 mg/1 mL syrup	5 or 10 mg 1x/d	6-11 mos: 2.5 mg 1x/d[2] 12-23 mos: 2.5 mg 1x/d-bid[2] 2-5 yrs: 2.5 or 5 mg 1x/d or 2.5 mg bid 6-11 yrs: 5-10 mg 1x/d
Zyrtec (McNeil Consumer)			
Cetirizine/pseudoephedrine[1] generic	5 mg/120 mg ER tabs	1 tab bid	≥12 yrs: 1 tab bid
Zyrtec-D 12 hour (McNeil Consumer)			
Desloratadine – *Clarinex* (Schering-Plough)	5 mg tabs; 0.5 mg/mL syrup 2.5, 5 mg disintegrating tabs	5 mg 1x/d	6-23 mos: 1 mg 1x/d[3] 2-5 yrs: 1.25 mg 1x/d 6-11 yrs: 2.5 mg 1x/d
Desloratadine/pseudoephedrine			
Clarinex-D 12 hour (Schering-Plough)	2.5 mg/120 mg ER tabs	1 tab bid	≥12 yrs: 1 tab bid
Clarinex-D 24 hour	5 mg/240 mg ER tabs	1 tab 1x/d	≥12 yrs: 1 tab 1x/d
Fexofenadine – generic	30, 60, 180 mg tabs	60 mg bid or 180 mg 1x/d	6-23 mos: 15 mg bid[3] 2-11 yrs: 30 mg bid
Allegra (Sanofi-aventis, PD-RX)	60, 80 mg tab; 30 mg/5 mL susp; 30 mg disintegrating tab		
Fexofenadine/pseudoephedrine			
Allegra-D 12 hour (Sanofi-aventis, and others)	60 mg/120 mg ER tabs	1 tab bid	≥12 yrs: 1 tab bid
Allegra-D 24 hour	180 mg/240 mg ER tabs	1 tab 1x/d	≥12 yrs: 1 tab 1x/d
Levocetirizine – *Xyzal* (Sanofi-aventis, UCB)	5 mg tabs; 0.5 mg/mL oral solution	5 mg 1x/d	6 mos-5yrs: 1.25 mg 1x/d[4] 6-11 yrs: 2.5 mg 1x/d
Loratadine[2] – generic	10 mg tabs; 10 mg disintegrating tabs; 1 mg/mL syrup and susp	10 mg 1x/d	2-5 yrs: 5 mg 1x/d ≥6 yrs: 10 mg 1x/d
Claritin (Schering-Plough)	10 mg tabs; 1 mg/mL syrup; 5, 10 mg disintegrating tabs; 10 mg caps		
Alavert (Wyeth)	10 mg tabs; 10 mg disintegrating tabs		
Loratadine/pseudoephedrine[1]			
Claritin-D 12 hour (Schering-Plough)	5 mg/120 mg ER tabs	1 tab bid	≥12 yrs: 1 tab bid
Claritin-D 24 hour	10 mg/240 mg ER tabs	1 tab 1x/d	≥12 yrs: 1 tab 1x/d
Alavert-D 12 hour (Wyeth)	5 mg/120 mg ER tabs	1 tab bid	≥12 yrs: 1 tab bid
Leukotriene Receptor Antagonist			
Montelukast – *Singulair* (Merck)	10 mg tabs; 4, 5 mg chew tabs; 4 mg granule packets	10 mg 1x/d	6 mos-5 yrs: 4 mg 1x/d 6-14 yrs: 5 mg 1x/d

1. Available without a prescription.
2. Only approved for treatment of chronic idiopathic urticaria and perennial allergic rhinitis in this age group.
3. Only approved for treatment of chronic idiopathic urticaria in this age group.
4. Not approved for treatment of seasonal allergic rhinitis in children <2 years old.

prevention and relief of allergic rhinitis symptoms and are the drugs of choice for treatment of moderate to severe disease. All of these agents reduce sneezing, itching, discharge and congestion. Most are effective when given once daily. There is no clear dose-response relationship with these drugs, suggesting that currently recommended doses are already at the plateau of the dose-response curve. Although the onset of action generally occurs within 12 hours, they may take 7 days or more to be maximally effective. Intranasal corticosteroid sprays may be effective in decreasing ocular as well as nasal symptoms of seasonal allergic rhinitis.[8,9]

Adverse effects of intranasal corticosteroid treatment are mild; they include dryness and irritation, burning or bleeding of the nasal mucosa, sore throat, epistaxis and headache. Sensory attributes of intranasal corticosteroid formulations such as odor and aftertaste may affect patient compliance.[10]

Intranasal corticosteroids used as directed generally do not cause atrophy of the nasal mucosa. Growth suppression has been reported with use of intranasal beclomethasone dipropionate bid for 12 months in children 6-9 years old, but not with newer intranasal corticosteroids such as ciclesonide, fluticasone propionate or mometasone.[11] Because many patients may require long-term treatment with corticosteroids by various routes (intranasal for rhinitis, inhaled orally for asthma, and applied topically for atopic dermatitis), it is important with all routes to prescribe the lowest dose that prevents and controls symptoms.

Table 2. Some Nasal Sprays for Allergic Rhinitis

Drug	Formulations	Usual Daily Adult Dosage	Usual Daily Pediatric Dosage
H_1 -Antihistamine			
Azelastine – *Astelin* 0.1%(Meda)	Metered-dose pump spray (137 mcg/spray)	1-2 sprays per nostril 2x/d	5-11 yrs: 1 spray per nostril 2x/d
Astepro 0.1% (Meda)[1]	Metered-dose pump spray (137 mcg/spray)	1-2 sprays per nostril 2x/d	≥12 yrs: 1-2 sprays per nostril 2x/d
Astepro 0.15%	Metered-dose pump spray (205.5 mcg/spray)	1-2 sprays per nostril 2x/d[2]	≥12 yrs: 1-2 sprays per nostril 1-2x/d
Olopatadine – *Patanase* (Alcon)	Metered-dose pump spray (665 mcg/spray)	2 sprays per nostril 2x/d	≥12 yrs: 2 sprays per nostril 2x/d
Corticosteroids			
Beclomethasone dipropionate *Beconase AQ* (GSK)	Metered-dose pump spray (42 mcg/spray)	1-2 sprays per nostril 2x/d	≥6 yrs: 1-2 sprays per nostril 2x/d
Budesonide – *Rhinocort Aqua* (AstraZeneca)	Metered-dose pump spray (32 mcg/spray)	1-4 sprays per nostril 1x/d	6-11 yrs: 1-2 sprays per nostril 1x/d
Ciclesonide – *Omnaris* (Sepracor/Nycomed)	Metered-dose pump spray (50 mcg/spray)	2 sprays per nostril 1x/d	≥6 yrs[3]: 2 sprays per nostril 1x/d
Flunisolide generic	Metered-dose pump spray (25 mcg/spray)	2 sprays per nostril bid-tid	6-14 yrs: 1 spray per nostril tid or 2 sprays per nostril 2x/d
Fluticasone furoate – *Veramyst* (GSK)	Metered-dose pump spray (27.5 mcg/spray)	2 sprays per nostril 1x/d	2-11 yrs: 1-2 sprays per nostril 1x/d
Fluticasone propionate generic *Flonase* (GSK)	Metered-dose pump spray (50 mcg/spray)	1-2 sprays per nostril 1x/d or 1 spray per nostril 2x/d	≥4 yrs: 1-2 sprays per nostril 1x/d
Mometasone furoate *Nasonex* (Schering-Plough)	Metered-dose pump spray (50 mcg/spray)	2 sprays per nostril 1x/d	2-11 yrs: 1-2 sprays per nostril 1x/d
Triamcinolone acetonide *Nasacort AQ* (Sanofi-Aventis)	Metered-dose pump spray (55 mcg/spray)	2 sprays per nostril 1x/d	2-5 yrs: 1 spray per nostril 1x/d 6-11 yrs: 1-2 sprays per nostril 1x/d
Mast-Cell Stabilizer			
Cromolyn sodium – *Nasalcrom*[4] (Pfizer Consumer)	Metered-dose pump spray (5.2 mg/spray)	1 spray per nostril tid-qid	≥2 yrs: 1 spray per nostril tid-qid
Anticholinergic			
Ipratropium bromide generic *Atrovent* (Boehringer Ingelheim)	Metered-dose pump spray (21 or 42 mcg/spray) (21 or 42 mcg/spray)	2 sprays per nostril bid-qid	≥5 yrs: 2 sprays per nostril bid-qid

1. FDA approved for the treatment of seasonal allergic rhinitis.
2. Dosage for seasonal allergic rhinitis is 1-2 sprays per nostril bid or 2 sprays per nostril once daily. Dosage for perennial allergic rhinitis is 2 sprays per nostril bid.
3. Not approved for treatment of perennial allergic rhinitis in children <12 years old.
4. Available without a prescription.

Leukotriene Receptor Antagonist – Cysteinyl leukotrienes are released in the nasal mucosa during allergic inflammation and produce nasal congestion. Montelukast *(Singulair)*, the only leukotriene receptor antagonist FDA-approved for use in seasonal and perennial allergic rhinitis, has a modest effect in relieving sneezing, itching, discharge and congestion, but it is less effective than intranasal corticosteroids. The combination of a leukotriene receptor antagonist and an H_1-antihistamine is superior to either used alone.

Decongestants – Decongestants act as vasoconstrictors in the nasal mucosa primarily through stimulation of alpha-1 adrenergic receptors on venous sinusoids. They are effective only for relief of congestion, and not for sneezing, itching or discharge. Some oral formulations containing pseudoephedrine are being removed from the market because of concerns about illicit use. Substitutes containing phenylephrine (*Sudafed PE*, and others) may not be effective.[12]

Adverse effects of oral decongestants include insomnia, excitability, headache, nervousness, anorexia, palpitations, tachycardia, arrhythmias, hypertension, nausea, vomiting and urinary retention. Pseudoephedrine should be used cautiously in patients with cardiovascular disease, hypertension, diabetes, hyperthyroidism, closed-angle glaucoma or bladder neck obstruction.

Topical intranasal decongestants are less likely than oral drugs to cause systemic effects, but they may cause stinging, burning, sneezing and dryness of the nose and throat. In order to avoid rebound congestion, they should not be used for more than three consecutive days. Rhinitis medicamentosa associated with prolonged use of topical drugs is treated by discontinuing the topical decongestant and administering intranasal corticosteroids to control symptoms.[13]

Mast-Cell Stabilizer – Cromolyn sodium, given before allergen exposure, inhibits mast cell degranulation and mediator release. It is sometimes used for prophylaxis of allergic rhinitis symptoms, but is considerably less effective than intranasal corticosteroids and must be used 4 times a day. Cromolyn sodium has virtually no local or systemic toxicity.

Anticholinergic – Ipratropium bromide is a quaternary amine antimuscarinic agent. Given as a nasal spray, it is poorly absorbed systemically and does not readily cross the blood-brain barrier. Ipratropium is useful in patients whose primary symptom is nasal discharge, for example after exposure to irritants or cold air, or as an adjunct to reduce rhinorrhea not controlled by other medications. It does not relieve sneezing, itching or nasal congestion. Ipratropium may cause dry nose and mouth, pharyngeal irritation, urinary retention and, with inadvertent instillation in the eye, increases in intraocular pressure. It should be used with caution in patients with glaucoma and in those with prostatic hypertrophy or bladder neck obstruction.

Omalizumab (Anti-IgE Antibody) – Omalizumab *(Xolair)*, which is injected subcutaneously for treatment of allergic asthma[14], decreases free IgE levels in serum, the number of IgE receptors on mast cells and basophils, and the nasal response to allergens. It has a dose-dependent beneficial effect in seasonal allergic rhinitis; how its efficacy compares to that of H_1-antihistamines and intranasal corticosteroids remains to be determined. Omalizumab is generally well tolerated, but rarely causes anaphylaxis. It has not been approved by the FDA for treatment of allergic rhinitis.

Systemic Corticosteroids – Patients with severe allergic rhinitis who do not respond to, or are intolerant of, other drugs are sometimes treated with oral corticosteroids, a last resort that should be avoided if possible.

Complementary and Alternative Treatments – Herbal remedies, homeopathy and acupuncture are widely used for allergic rhinitis symptoms, but their efficacy has not been established.[15]

Pregnancy – Drugs used in allergic rhinitis for which safety in pregnancy has been demonstrated include intranasal corticosteroids, the H_1-antihistamines cetirizine and loratadine, the topical ophthalmic H_1-antihistamine emedastine, the leukotriene receptor antagonist montelukast and the mast-cell stabilizer cromolyn sodium.

Drugs of Choice – For mild to moderate allergic rhinitis, especially for seasonal or intermittent symptoms, an oral second-generation H_1-antihistamine or an intranasal H_1-antihistamine is a reasonable choice. For moderate to severe allergic rhinitis, an intranasal corticosteroid is more likely to be effective. No single oral second-generation H_1-antihistamine or intranasal corticosteroid has been convincingly demonstrated to be superior to any other within the same class.

ALLERGIC CONJUNCTIVITIS

Allergic conjunctivitis, the most common form of ocular allergy, is often associated with seasonal allergic rhinitis. The main symptom, itching, is usually relieved by an **oral H_1-antihistamine**, preferably a second-generation, minimally or nonsedating drug such as cetirizine, desloratadine, fexofenadine, levocetirizine or loratadine.[16] **Antihistamine eye drops** are also effective, and have a more rapid onset of action (within a few minutes). Ketotifen (which is available over the counter), azelastine, bepotastine, epinastine and olopatadine are marketed as having both H_1-antihistamine and mast-cell-stabilizing activity, but all H_1-antihistamines probably have some mast-cell-stabilizing activity. Ophthalmic **stabilizers** cromolyn, lodoxamide, nedocromil and pemirolast have a slower onset of action than H_1-antihistamines, and are mostly used for treatment of mild to moderate symptoms.[17] The topical nonsteroidal anti-inflammatory drug ketorolac can also be used, but in comparative studies it was less effective than olopatadine or emedastine.[18]

Topical ophthalmic decongestants reduce erythema, congestion, itching and eyelid edema, but are not drugs of choice because of their short duration of action and adverse effects, including burning, stinging, rebound hyperemia and conjunctivitis medicamentosa. Because

Table 3. Some Ophthalmic Drugs for Allergic Conjunctivitis

Drug	Some Formulations	Available Sizes	Usual Daily Dosage	Pediatric Age Range
H_1-Antihistamines				
Emedastine difumarate *Emadine* (Alcon)	0.05% soln*	5 mL	1 drop qid	≥3 yrs
Mast-Cell Stabilizers				
Cromolyn sodium[1] – generic	4% soln*	10 mL	1-2 drops q4-6h	>4 yrs
Lodoxamide tromethamine *Alomide*[1] (Alcon)	0.1% soln*	10 mL	1 drop qid	>2 yrs
Nedocromil *Alocril* (Allergan)	2% soln*	5 mL	1-2 drops bid	>3 yrs
Pemirolast potassium *Alamast* (Vistakon)	0.1% soln**	10 mL	1-2 drops qid	≥3 yrs
H_1-Antihistamines and Mast-Cell Stabilizers				
Azelastine *Optivar* (Meda)	0.05% soln*	6 mL	1 drop bid	≥3 yrs
Bepotastine *Bepreve* (Ista)	1.5% soln*	10 mL	1 drop bid	≥2 yrs
Epinastine *Elestat* (Allergan)	0.05% soln*	5 mL	1 drop bid	≥3 yrs
Ketotifen fumarate[2] – generic	0.025% soln*	5 mL	1 drop q8-12h	≥3 yrs
Zaditor (Novartis)	0.025% soln*	5 mL	1 drop q8-12h	≥3 yrs
Claritin Eye (Schering-Plough)	0.025% soln*	5 mL	1 drop q8-12h	≥3 yrs
Eye Itch Relief (Major)	0.025% soln*	5 mL	1 drop q8-12h	≥3 yrs
Olopatadine – *Pataday* (Alcon)	0.2% soln*	2.5 mL	1 drop 1x/d	≥3 yrs
Patanol (Alcon)	0.1% soln*	5 mL	1-2 drops bid	≥3 yrs
Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)				
Ketorolac tromethamine – generic *Acular* (Allergan)	0.5% soln*[3]	3, 5, 10 mL	1 drop qid	≥3 yrs

* Contains benzalkonium chloride. ** Contains lauralkonium chloride, which may cause irritation.
1. Approved by the FDA for treatment of vernal keratoconjunctivitis, vernal conjunctivitis and vernal keratitis.
2. Available over the counter.
3. Also available in 0.4% soln for use in incisional refractive surgery.

of these effects, **antihistamine/decongestant combination eye drops** available over the counter such as pheniramine/naphazoline (*Visine A*, and others) and antazoline/naphazoline (*Vasocon-A*) are not good choices either, except for very short-term use in mild disease.

Patients who find that application of any topical ophthalmic preparation leads to stinging or burning should try refrigerating the drug before use. **Intranasal corticosteroid sprays** may also help relieve symptoms of allergic conjunctivitis.[19]

Topical **ophthalmic corticosteroids** should be considered a last resort in extreme situations. A corticosteroid that is inactivated rapidly in the anterior chamber, such as rimexolone (*Vexol*) or low-dose loteprednol etabonate (*Alrex, Lotemax*), is preferred. Duration of treatment should be limited to 1-2 weeks. The patient should be monitored by an ophthalmologist because these medications have been associated with exacerbations of viral infections of the conjunctiva and cornea, increased intraocular pressure and cataract formation.

Drugs of Choice – Any second-generation oral H_1-antihistamine or topical ophthalmic H_1-antihistamine/mast-cell stabilizer is effective and safe for the treatment of allergic conjunctivitis.

ATOPIC DERMATITIS

Treatment of atopic dermatitis/eczema includes hydration and moisturization, topical anti-inflammatory agents such as corticosteroids and calcineurin inhibitors, as well as anti-infective therapy.[20]

Topical Corticosteroids – A medium- or high-potency topical corticosteroid may be needed to control skin inflammation in atopic dermatitis, but for maintenance treatment the topical corticosteroid with the lowest potency that is effective in a given patient should be used. High-potency corticosteroids such as betamethasone dipropionate 0.05% ointment/cream should never be used on the face; even on the trunk and extremities, they should be used only for short periods of time. Low-potency corticosteroids such as hydrocortisone cream can be used safely on the face and intertriginous areas.

Table 4. Some Topical Drugs for Atopic Dermatitis

Drug	Vehicle
CALCINEURIN INHIBITORS	
Pimecrolimus 1%	
Elidel (Novartis)	cream
Tacrolimus 0.03%	
Protopic (Astellas)	oint
Tacrolimus 0.1%	
Protopic (Astellas)	oint
CORTICOSTEROIDS	
Super-High Potency	
Betamethasone dipropionate	
augmented 0.05% – generic	oint, lotion, gel
Diprolene (Schering-Plough)	oint, gel
Clobetasol propionate 0.05%	
generic	cream, oint, gel, foam, soln
Cormax (Watson)	oint, soln
Clobex (Galderma)	lotion, spray, shampoo
Olux (Connetics Corp)	foam
Temovate (GSK)	cream, soln, oint, gel
Fluocinonide 0.1%	
Vanos (Medicis)	cream
Halobetasol propionate 0.05%	
generic	cream, oint
Ultravate (Ranbaxy)	cream, oint
High Potency	
Amcinonide 0.1% – generic	oint
Betamethasone	
dipropionate 0.05%	
augmented – generic	cream
Diprolene AF (Schering-Plough)	cream
Betamethasone	
dipropionate 0.05%	
generic	oint
Desoximetasone 0.25%	
generic	cream, gel, oint
Topicort (Taro)	cream, gel, oint
Desoximetasone 0.05%	
generic	gel
Topicort 0.05% (Taro)	gel
Diflorasone diacetate 0.05%	
generic	oint
Fluocinonide 0.05%	
generic	gel, oint, soln cream
Halcinonide 0.1%	
Halog (Ranbaxy)	cream, oint
Mometasone furoate 0.1%	
generic	oint
Elocon (Schering-Plough)	oint
Triamcinolone acetonide 0.5%	
generic	oint

Table 4. Some Topical Drugs for Atopic Dermatitis (cont.)

Drug	Vehicle
Medium-High Potency	
Amcinonide 0.1%	
generic	cream, lotion
Betamethasone dipropionate 0.05%	
generic	cream
Betamethasone	
valerate 0.1% – generic	oint
Desoximetasone 0.05%	
generic	cream
Diflorasone	
diacetate 0.05%	
generic	cream
Fluocinonide	
emollient 0.05%	
generic	cream
Fluticasone propionate 0.005%	
generic	oint
Cutivate (PharmDerm)	
Triamcinolone	
acetonide 0.1%	
generic	oint
Triamcinolone acetonide 0.5%	
generic	cream
Medium Potency	
Betamethasone valerate 0.12%	
Luxiq (Stiefel Labs)	foam
Fluocinolone	
acetonide 0.025%	
generic	oint
Hydrocortisone	
valerate 0.2%	
generic	oint
Westcort (Ranbaxy)	oint
Mometasone furoate 0.1%	
generic	cream, lotion
Elocon (Schering-Plough)	cream, lotion
Triamcinolone acetonide 0.1%	
generic	cream
Medium-Low Potency	
Betamethasone dipropionate 0.05%	
generic	lotion
Betamethasone valerate 0.1%	
generic	cream
Desonide 0.05%	
generic	oint
Desowen (Galderma)	
Fluocinolone acetonide 0.025%	
generic	cream
Flurandrenolide 0.05%	
Cordran (Aqua)	lotion
Cordran SP (Aqua)	cream
Fluticasone propionate 0.05%	
generic	cream
Cutivate (PharmaDerm)	

Local adverse effects of topical corticosteroids include development of striae and skin atrophy. Used on the eyelids for prolonged periods, they can cause glaucoma and cataracts. Systemic side effects relate to corticosteroid potency, site of application, percentage of body surface covered and duration of treatment. The potential for adrenal suppression is greatest with high-potency corticosteroids or when corticosteroids are applied under occlusive dressings, especially in infants and young children with widespread skin involvement who require long-term treatment. The risk of skin and other lymphomas also increases with the potency of the topical corticosteroids used and the duration of exposure.[21]

Topical Calcineurin Inhibitors – The topically applied calcineurin inhibitors tacrolimus and pimecrolimus are microbial-derived macrolides with a

Table 4. Some Topical Drugs for Atopic Dermatitis (cont.)

Drug	Vehicle
Medium-Low Potency (continued)	
Hydrocortisone butyrate 0.1%	
generic	cream, oint, soln
Locoid (Triax)	cream
	oint, soln
Locoid Lipocream (Triax)	cream
Hydrocortisone valerate 0.2%	
generic	cream
Prednicarbate 0.1% – generic	cream
Dermatop (Dermik)	
Triamcinolone acetonide 0.025%	
generic	oint
Triamcinolone acetonide 0.1%	
generic	lotion
Low Potency	
Alclometasone dipropionate 0.05%	
generic	cream, oint
Aclovate (GSK)	cream, oint
Betamethasone valerate 0.1%	
generic	lotion
Clocortolone 0.1%	
Cloderm (Valeant)	cream
Desonide 0.05%	
generic	cream, lotion
Desonate (Intendis)	gel
DesOwen (Galderma)	cream, lotion
Verdeso (Stiefel Labs)	foam
Fluocinolone acetonide 0.01%	
generic	cream, soln
Triamcinolone acetonide 0.025%	
generic	cream, lotion
Lowest Potency (may be ineffective for some indications)	
Hydrocortisone 0.5%[1]	
generic	cream, oint, lotion
Hydrocortisone 1.0%[1]	
generic	cream, oint, lotion
Hydrocortisone 2.5%	
generic	cream, oint, lotion

1. Available without a prescription.

mechanism of action similar to that of cyclosporine (*Sandimmune*, and others). They can reduce itching and inflammation within a few days. Topical tacrolimus 0.1% is similar in efficacy to a topical corticosteroid with moderate potency and might be considered for long-term use in patients with topical corticosteroid-resistant atopic dermatitis, especially at sites such as the face or intertriginous areas where adverse effects from topical corticosteroid toxicity may be troublesome. Pimecrolimus is not as effective as a moderately potent topical corticosteroid, but it is an effective steroid-sparing therapy for mild to moderate atopic dermatitis.[22] Intermittent applications of 0.03% tacrolimus ointment 3 times weekly appear to increase the number of flare-free days and the time to relapse.[23]

Adverse effects, generally mild, include transient local itching, burning, stinging or erythema and a temporary increase in skin infections. Pimecrolimus is less likely than tacrolimus to cause these effects. These drugs do not cause cutaneous atrophy, and they can be used on the face, including areas around the mouth and eyes, and on the axillae and groin. Data are available showing that tacrolimus has been used safely in adults and children 2-15 years old for up to 4 years. In 2005, reports of malignancies in animals given large doses and of 8 skin malignancies and 12 lymphomas in adults and children treated with these drugs (not significantly higher than expected) prompted the FDA to issue a public health advisory about potential long-term risks of malignancy with topical tacrolimus and pimecrolimus. A retrospective cohort study found an increased risk of T-cell lymphoma among patients exposed to tacrolimus.[24] More long-term data are needed.[25]

Coal Tar – Coal tar preparations have anti-pruritic and anti-inflammatory effects, but they are messy and are now seldom recommended except in shampoo formulations. Adverse effects include skin irritation, folliculitis and photosensitivity.

Systemic Drugs – In many patients with atopic dermatitis, H_1-antihistamines are not very effective in relieving itching, probably because in addition to histamines, other mediators such as neuropeptides and cytokines also contribute to itching. Cetirizine, although not FDA-approved for this indication, was mildly effective and reduced the use of topical steroids in one 18-month study in infants with atopic dermatitis.[26]

Short courses of an oral corticosteroid such as prednisone may be needed in severe acute exacerbations of atopic dermatitis, but the drug should be tapered quickly, and intensified skin care with topical corticosteroids and calcineurin inhibitors should be started before tapering to reduce rebound inflammation. In patients with recalcitrant atopic dermatitis, cyclosporine and other immunomodulators have been used.

Anti-Infective Therapy – If a secondary infection with *Staphylococcus aureus* is present, a semi-synthetic penicillin or a first-generation cephalosporin such as cephalexin can be given for 7-10 days. Maintenance antibiotic treatment should be avoided because it may result in colonization by methicillin-resistant organisms. The topical anti-staphylococcal antibiotic mupirocin (*Bactroban*) applied three times daily to affected areas for 7-10 days may be effective. Twice-daily treatment for 5 days with a nasal preparation of mupirocin may reduce intranasal carriage of *S. aureus*.[27]

Nonpharmacologic Treatment – Skin hydration with application of moisturizers and emollients is important. Products containing ceramides such as *CeraVe* are reported to be more efficacious than traditional moisturizers.[28,29] Avoidance of irritating soaps, detergents or clothing, dust mites, extremes of temperature and humidity or anything else that triggers the itch/scratch cycle, plus trimming of fingernails, are all helpful in the management of atopic dermatitis. Identification and elimination of foods that exacerbate atopic dermatitis may sometimes also be helpful. Phototherapy has been effective in some patients. Allergen-specific immunotherapy is not recommended for treatment of atopic dermatitis.[20]

Drugs of Choice – Topical corticosteroid creams and ointments remain first-line choices for pharmaco-therapy of atopic dermatitis. Pimecrolimus appears to be an effective steroid-sparing therapy for mild to moderate disease. Tacrolimus might be able to replace a potent corticosteroid for long-term treatment, especially on the face or intertriginous areas. Pimecrolimus generally costs slightly less than tacrolimus, but much more than generic topical corticosteroids.

URTICARIA

Acute urticaria is a self-limited condition that responds well to treatment with an H_1-antihistamine, preferably a second-generation drug such as cetirizine, fexofenadine, loratadine, desloratadine or levocetizirine.[30-32]

Chronic urticaria can last for months, years or even decades. Oral H_1-antihistamines decrease itching and reduce the number, size and duration of wheals. Taken regularly, they can prevent new wheals from appearing. Higher doses of a second-generation H_1-antihistamine are now recommended by some specialists for the treatment of chronic urticaria that does not respond to usual recommended doses.[33] First-generation sedating antihistamines such as diphenhydramine or hydroxyzine are still used for urticaria, but controlled trials are lacking.

The leukotriene receptor antagonist montelukast, alone or added to an H_1-antihistamine such as loratadine, has been effective against urticaria in some studies, but not in others. Topical corticosteroid creams and ointments are not effective in chronic urticaria. Short-term treatment with an oral corticosteroid or cyclosporine may be required in some patients.[34] Low doses of cyclosporine have been effective in patients with urticaria unresponsive to antihistamines.[35]

Patients should avoid nonspecific exacerbating factors for urticaria such as anything that raises body temperature. Patients with urticaria triggered by aspirin or other NSAIDs should not take these medications. Patients with known physical urticaria triggers such as cold, heat, light, or pressure should avoid them.[30]

The pathophysiologies of **urticarial vasculitis** and **nonallergic angioedema,** including hereditary angioedema, are different from that of urticaria, and these diseases do not respond to conventional H_1-antihistamine treatment.[36]

ANAPHYLAXIS

Patients at risk for anaphylaxis should receive printed information about how to avoid confirmed relevant trigger factors, such as food or drugs. The Food Allergy and Anaphylaxis Network (www.foodallergy.org) provides support for patients with food allergies. If stinging insects are the trigger for anaphylaxis, patients should be referred to a specialist for venom immunotherapy, which provides long-lasting, potentially life-saving protection.[37]

All patients at risk of anaphylaxis should be equipped with epinephrine auto-injectors such as *EpiPen* or *Twinject*, which provide epinephrine in fixed doses of 0.15 mg and 0.3 mg. The recommended dose of epinephrine is 0.01 mg/kg intramuscularly (maximum 0.5 mg). Auto-injectors containing 0.15 mg are, therefore, optimal for young children weighing around 15 kg, and those containing 0.3 mg for children weighing 30 kg or more. Since no weight-appropriate dose for infants is available in an auto-injector, many physicians prescribe the 0.15 mg auto-injector (off-label) for this age group. Since no auto-injector provides an optimal dose for most children weighing between 15 and 30 kg, some physicians prescribe auto-injectors containing 0.3 mg epinephrine for children who have attained a weight of 22 or 23 kg.[38] Patients and caregivers need to be trained to use auto-injectors correctly and safely.[39]

Absorption of epinepherine after intramuscular injection is faster and the effect is less variable than after subcutaneous injection, but the needle lengths of *EpiPen* and *Twinject* may be too short for an intramuscular injection in some patients, including children.[40] After injection of epinephrine, patients should be taken to the nearest emergency department and observed after apparent recovery because, despite no further exposure to the trigger, anaphylaxis symptoms may recur within 72 hours in up to 20% of patients.[41] H_1-antihistamines are often used to treat anaphylaxis, but they do not prevent or relieve airway obstruction, hypotension or shock.

LARGE LOCAL ALLERGIC REACTIONS

Large local allergic reactions occurring, for example, at the sites of insect stings or bites appear within 24 hours. Although they may last for 5-7 days, they are self-limited. Local application of cold compresses and an oral second-generation H_1-antihistamine such as cetirizine may relieve itching. The H_1-antihistamine can be supplemented, if needed, with application of a topical corticosteroid cream to the skin for a few days. For severe large local reactions, oral prednisone 1 mg/kg, up to 50 mg daily for 5-7 days, should be prescribed. Venom immunotherapy can prevent anaphylactic and large local reactions to insect stings in patients who have had severe reactions and cannot avoid exposure to stinging insects.[42]

IMMUNOTHERAPY

Allergen-specific immunotherapy involving injection of gradually increasing doses of the causative allergen ("allergy shots") is effective in allergic rhinitis and allergic conjunctivitis (and in allergic asthma).[43,44] Standard subcutaneous allergen immunotherapy is limited by the potential for adverse effects, including anaphylaxis, and the requirement for regular (usually monthly) maintenance dosing for several years, but the benefits can persist for years after treatment is stopped. Insect venom immunotherapy is highly effective in preventing anaphylaxis triggered by stings from honeybees, yellow jackets, hornets and wasps.[45] Fire ant whole body extract immunotherapy can also protect against anaphylaxis. Sublingual immunotherapy for treatment of allergic rhinitis and allergic conjunctivitis due to airborne allergens is used in Europe and is currently being studied in the US and Canada. It appears to be effective.[46]

CONCLUSION

For treatment of **allergic rhinitis**, topical intranasal corticosteroids are the most effective drugs available. An oral second-generation H_1-antihistamine or an intranasal H_1-antihistamine is a good choice for mild to moderate symptoms. For **allergic conjunctivitis**, an oral second-generation H_1-antihistamine or a topical ophthalmic H_1-antihistamine/mast-cell stabilizer can be used. Allergen-specific immunotherapy is effective for both of these disorders, and the benefits can last for years after therapy is stopped.

In patients with **atopic dermatitis**, a topical corticosteroid with the lowest potency that relieves inflammation would be a cost-effective choice. The calcineurin inhibitors pimecrolimus (*Elidel*) and tacrolimus (*Protopic*) have the advantage over topical corticosteroids of not causing skin atrophy, adrenal suppression or ocular adverse effects, and are particularly useful on the face, but they are expensive and their long-term safety remains to be determined.

In acute and chronic **urticaria**, oral second-generation H_1-antihistamines are the most effective drugs for symptom relief. Topical corticosteroids are not effective.

Patients at **risk of anaphylaxis** recurrence should be equipped with epinephrine auto-injectors and taught when and how to use them.

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Issue 90 Questions

1. For the treatment of allergic rhinitis, H_1-antihistamines are least effective in relieving:
   a. sneezing
   b. itching
   c. discharge
   d. nasal congestion

   Pg. 9

2. First-generation H_1-antihistamines sold for the relief of cough, colds, allergies and insomnia are no longer approved in the US for children:
   a. < 6 months old
   b. < 1 year old
   c. < 2 years old
   d. < 6 years old

   Pg. 9

3. Second-generation H_1-antihistamines are:
   a. used as first-line therapy in patients with mild-moderate allergic rhinitis
   b. more likely to have CNS adverse effects than first-generation antihistamines
   c. no longer approved for use in children < 6 years old
   d. being taken off the market because of concerns about abuse potential

   Pg. 9

4. The drugs of choice for the treatment of moderate to severe allergic rhinitis are:
   a. oral first-generation H_1-antihistamines
   b. intranasal corticosteroids
   c. leukotriene receptor antagonists
   d. decongestants

   Pg. 9/10

5. The only leukotriene receptor antagonist FDA-approved for use in seasonal and perennial allergic rhinitis is:
   a. azelastine
   b. olopatadine
   c. montelukast
   d. cetirizine

   Pg. 11

6. Decongestants are effective only for relief of:
   a. sneezing
   b. discharge
   c. itching
   d. congestion

   Pg. 11

7. Drugs for treatment of allergic conjunctivitis include:
   a. second-generation oral H_1-antihistamines
   b. topical ophthalmic H_1-antihistamines
   c. mast-cell stabilizers
   d. all of the above

   Pg. 12

8. Corticosteroids that can be used safely on the face and intertriginous areas include:
   a. low-potency corticosteroids
   b. high-potency corticosteroids
   c. super-high potency corticosteroids
   d. all of the above

   Pg. 13

9. Adverse effects of topical calcineurin inhibitors include:
   a. burning
   b. stinging
   c. erythema
   d. all of the above

   Pg. 15

10. Drugs of choice for treatment of urticaria include:
    a. oral H_1-antihistamines
    b. nonsteroidal anti-inflammatory agents
    c. super-potent topical corticosteroids
    d. all of the above

    Pg. 16

11. Absorption of epinephrine is faster and less variable in effect when administered:
    a. subcutaneously
    b. intravenously
    c. intramuscularly
    d. all of the above

    Pg. 16

12. Allergen-specific immunotherapy is effective for treatment of:
    a. allergic rhinitis
    b. allergic conjunctivitis
    c. allergic asthma
    d. all of the above

    Pg. 17

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